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THE CLINICAL DISPARITY OF GALLSTONE DISEASE IN A CHINESE OCCUPATIONAL POPULATION IN TAIPEI, TAIWAN

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ABSTRACT

Background/Aims: This study is conducted to discuss the disparity of gallstone disease (GSD) of a Chinese occupational population in Taipei, Taiwan.

Materials and Methods: There were 8,352 (5,243 men and 3,109 women) healthy participants admitted to a regional hospital for a healthy examination in 2009. Blood specimens and abdominal ultrasound characteristics were analyzed.

Results: The overall prevalence of GSD was estimated 3.89% and increased significantly with increasing age. The prevalence of GSD in women was not significantly higher than that in men (3.99% vs. 3.83%, p value for the ^{2} test=0.72). Multiple logistic regression analysis indicated that subjects' age [odds ratio (OR)=1.06, 95% confidence interval (CI)=1.05-1.07] and obesity [body mass index (BMI) ≥27 vs. <24 kg/m^2, OR=1.70, 95% CI=1.12-2.34] were significantly related to GSD. In subjects with a normal BMI, nonalcoholic fatty liver disease (NAFLD, OR=1.47, 95% CI=1.01-2.14) was statistical significantly related to present GSD. There was no association between NAFLD and GSD in overweight or obese subjects. The disparity of GSD among occupations was revealed.

Conclusion: Occupational populations with older age, higher BMI, and NAFLD should be considered symptomatic of GSD.

Introduction

Gallstone disease (GSD) is typically benign; however, GSD-associated complications influence essentially to health care expense and threaten subjects' life (1). The increasing prevalence of GSD and the epidemiological transition in the natural history of GSD warrant research in diverse geographical areas and exploration of predictors (2-5). This is especially essential due to a majority of associated factors for diagnosed GSD are possibly modifiable (2). Furthermore, cholecystectomy can be a treatment approach to GSD patients, and the quality-adjusted life years gained from this surgery is estimated 1.8 (0.09 × 20) if patients have a life expectancy of twenty years (6). A clearer knowledge of the associated factors could facilitate in identifying GSD patients and reducing the risk of GSD in some potential candidates (3).

The pathogenesis of GSD is multifactorial aetiology and probably develops from heterogeneous pathways between various genetic and environmental factors (7,8). Because of the high GSD prevalence and nonalcoholic fatty liver disease (NAFLD), co-occurrence is highly likely in many cases; moreover, NAFLD and GSD exhibit joint risk factors (9). GSD has viewed as one of the major preventive medicine concerns despite the ameliorated standard of living, and no consensus has been reached on the clinical implications of GSD. GSD and NAFLD both are related to metabolic factors, insulin resistance, and their coexistence would also be mediated pathogenically (7-9). Our review of the relevant literature shows that some ambiguousness exists regarding the morbidity of GSD and the characteristic of the association between obesity and NAFLD for GSD development. This study was designed to explore potential factors and to further meliorate the concerns of GSD pathogenesis. The study discussed the prevalence and the factors related to GSD in healthy occupational adults through a health screening program in Taipei, Taiwan.

Methods

Data resource

We conducted a cross-sectional study in 8,352 healthy occupational adults from different professional fields (5,243 men and 3,109 women) who voluntarily admitted to a regional hospital in the Northern Taiwan for a routine healthy examination from January, 1, 2009 to December, 31, 2009. Ultrasound results and data regarding age, sex, and demographics were analyzed. Fasting blood specimen were drawn through venipuncture by well-trained nurses. The using process to personal medical records, blood specimens, and ultrasound finding were approved by the Institutional Review Board of Cheng Hsin General Hospital (CHGH-IRB: (165)98-26) in Taipei, Taiwan. For the ethics consideration, eligible subjects were first asked whether they would be willing to participate and confirmed their willingness to participate by signing a consent form. All procedures adhered to the tenets of the Declaration of Helsinki. Patients' data were preserved confidential.

Definitions of criteria

On the basis of the Adult Treatment Panel III criteria (10,11), the criteria were defined as follows. Hypertension: high systolic blood pressure more than 135 mmHg or high diastolic blood pressure more than 85 mmHg, and high fasting plasma glucose more than 110 mg/dL; obesity: normal weight [body mass index (BMI) less than 24 kg/m^2], overweight (BMI between 24 and 27 kg/m^2), and obese (BMI more than 27 kg/m^2); hypercholesterolemia (200 mg/dL); hypertriglyceridemia (150 mg/dL); higher creatinine (1.5 mg/dL); higher alkaline phosphatase (95 U/L); and hyperuricemia (7 mg/dL for men or 6 mg/dL for women) (10,12,13). Serum alanine transaminase (ALT) or aspartate aminotransferase levels of more than 40 U/L were considered as elevated (14). In addition, the occupations were classified as follows: computer and mathematical occupations, architecture and engineering occupations, community and social service occupations, sales and related occupations, office and administrative support occupations, and production occupations (10).

Abdominal ultrasound screening

Trained ultrasonographists performed hepatic ultrasonography in all participants by using a TOSHIBA Nemio (SSA-550A) ultrasound

probe. A panel of radiologists examined the abdominal region after the subjects fasted for at least 8 h and diagnosed GSD on the basis of the presence of movable hyperechoic foci with acoustic shadows. GSD was then classified as single, multiple, and cholecystectomy, excluding gallbladder polyps. Cases were identified as any type of GSD study population (5).

The ultrasonographic findings used to diagnose NAFLD included echo discrepancy of liver and kidney, echo penetration into the deep portions of the liver, increased liver echogenicity, and clarity of the liver blood vessel structures (10). Participants who were diagnosed as having NAFLD in the outpatient department through ultrasound and without Wilson's disease history, intestinal bypass surgery, or gluten enteropathy; ingested drugs known to cause hepatic steatosis including methotrexate, tamoxifen, amiodarone, and nucleoside analogs; had a positive serology for hepatitis B or C virus; had other known liver diseases; and consumed alcohol (alcohol intake of ≥30 g/day for men and ≥20 g/day for women) were enrolled in this study (15).

Statistical analysis

Statistical analysis was performed by SPSS 17.0 (SPSS Inc., Chicago, IL, USA). The descriptive analysis of continuous and categorical variables are expressed as mean± standard deviation and percentages. A p value of less than 0.05 was considered statistically significant. Differences in specific proportions of GSD were evaluated using the x^2 trend test. The crude and adjusted odds ratios (ORs; adjusted for sex and subjects' age) and 95% confidence intervals (CIs) were estimated for the independent effects of factors related to prevalent GSD using multiple logistic regression.

Results

According to the ^{2} trend test results, the overall prevalence of GSD was estimated 3.89% (Table 1) and increased significantly with elder age (p<0.001). The prevalence of GSD in women was not substantially higher than that in men (3.99% vs. 3.83%, p value for the ^{2} test=0.72). Stratification by age into four broad groups revealed that the women participants exhibited a higher prevalence of GSD for all age groups, except for the 40- to 49-year age group, compared with the male participants. The ^{2} trend test indicated a significant positive association (p<0.001) between age and GSD in both men and women.

Figure 1 presents the disparity of prevalent GSD stratified by occupation. The prevalence rates of GSD in office and administrative support occupations, architecture and engineering occupations, production occupations, sales and related occupations, community and social service occupations, and computer and mathematical occupations were 2.40%, 3.97%, 3.38%, 4.35%, 4.13%, and 4.68%, respectively. In computer and mathematical occupations, architecture and engineering occupations, and community and social service occupations, men exhibited a higher GSD prevalence than did women.

Table 2 shows the crude and adjusted ORs for the relationship between particular relevant associated factors and GSD. Compared with subjects without GSD, subjects with GSD displayed a higher prevalence with respect to age, higher BMI, higher ALT, and NAFLD. Furthermore, the effects of independent associated factors on GSD stratified by BMI were examined based on the multiple logistic regression model (Table 3). After adjustments for confounding factors, age (OR=1.06, 95% CI=1.05–1.07) and obesity (BMI≥27 vs. <24 kg/m^2, OR=1.70, 95% CI=1.12–2.34) were found to be significantly related to GSD. In subjects with a normal BMI, NAFLD (OR=1.47, 95% CI=1.01–2.14) was significantly related to GSD. However, NAFLD was not significantly associated with GSD in overweight or obese subjects.

The disparity of GSD among the occupations was also explored by the multiple logistic regression model. After adjustment for confounders, older age, higher BMI, and NAFLD were found to be the common factors related to GSD (Table 4).

Discussion

Clinical implications of GSD

The estimated prevalence of GSD in this study was common at 3.89%. In previous studies, the prevalence of GSD varied with different study populations (3-5,7,9,16). In addition to the various methods used for GSD assessment, this disparity may be attributed to the differences among the sample populations (5). The relative lower prevalence observed in our findings may be attributed to the younger age of the subjects (<40 years, 4972/8352=59.5%). Another possible reason may be the occurrence of nondifferential misclassification-bias identification, which may lead to the underestimation of the prevalence of GSD. Furthermore, the different associated factors for GSD in each occupational profession imply that different health promotion strategies are essential to reduce the risk of GSD in occupational professions.

Early screening for GSD is crucial because ultrasonography could detect pre-clinical cases, thereby resulting in appropriate treatment and prevention of further advanced complications such as acute gallstone pancreatitis and gallbladder cancer (7). A relatively high prevalence of GSD among women was observed in this study. Some epidemiologic studies have reported pregnancy and sex hormones to be responsible for the high risk of GSD in females (2,16). However, the relationship between sex and GSD was not revealed statistical significant, implying that sex is a confounding factor due to its correlation with other potential clinical factors. In addition, consistent with the results of previous findings, older age was a significant associated factor for GSD (2,5,7). In elderly people, higher serum cholesterol are secreted by the liver and the catabolism of cholesterol to bile acid is reduced (5,17). GSD is least common in the prepubertal age (2,18). Long-term exposure to many risk factors, particularly in elderly people, may increase the risk of GSD (7,19). A sedentary lifestyle, which is more common among elderly people than in the younger population, may also increase the development of GSD (7). In concordance with previous findings, the prevalence of GSD did not differ significantly according to the type of occupation (3).

Consistent with the results of previous studies (1-3,5,7,18), our results show that obesity is strongly associated with GSD. Therefore, obesity is an indicator of the deterioration caused by GSD. In addition, we estimated the ORs for BMI in three categories to be 1.18 (95% CI=0.87–1.61) and 1.70 (95% CI=1.12–2.34) in the 24–27 kg/m^2 and ≥27 kg/m^2 groups, respectively, compared with the <24 kg/m^2 group. This finding suggests that the onset of GSD may be at a BMI of ≥27 kg/m^2 after the occurrence of a higher BMI. Several reports have also suggested that the relative risk of GSD was markedly higher in the most obese subjects (3). The risk of GSD in obese subjects may be higher because of the increased bile saturation resulting from an increased biliary cholesterol secretion, which possible depends on the higher cholesterol synthesis rate in these subjects (5,7).

NAFLD is a usual chronic liver disease triggered by complex components and its natural course ranges from asymptomatic indolent to the end stages of liver disease (10,20). Theoretically, NAFLD patients might be prone to GSD caused by impaired gallbladder motility and increased bile lithogenicity (21). However, the NAFLD–GSD association remains uncertain considering that it has been reported in only certain studies (21,22). Patients with nonalcoholic steatohepatitis have a increased prevalence of small intestinal bacterial overgrowth, as assessed using the C-D-xylose-lactulose breath test, and more tumor necrosis factor-a levels, compared with control subjects (23,24). Such changes may reflect a diminished fiber intake in NAFLD patients, which in turn, may decrease the intestinal transit time and increase biliary deoxycholic acid, leading to bile sovrasaturation and gallstone formation; this is an additional mechanism of the NAFLD to GSD association (24-26). Our data confirm the association between GSD and NAFLD in the normal BMI subgroup. NAFLD of unspecified etiology is an independent positive predictor of GSD, and this finding is probably linked to the inverse relationship linking body weight. Thus, we hypothesize that subjects with a normal BMI who take measures to prevent NAFLD have a lower risk of GSD. However, this hypothesis remains speculative and must be verified in prospective studies.

Perceived limitations

The major drawback of this study is based on the hospital-based study design, the potential self-selection bias is inevitable. The results of this study could not represent of the entire general population. Second, we screened the occupational population from only one area, however, this study retains higher statistical power to estimate the various associated factors for GSD given the relatively large study population. Third, cholesterol GSD is usual in Western countries, whereas pigment GSD is observed predominantly in Taiwan (5). Because we did not consider the distinction two types stones, some measurement errors and different pathogenicities may be observed. Fourth, we did not investigate the number of subjects with progression of liver disease and the clinical relationship between GSD and advanced liver disease. Finally, our results were conducted at a cross-section in time and therefore could not be used to explore long-term effects of demographic or biochemical factors, which might be critical influencers of GSD development. Prospective longitudinal analogous studies are warranted to complement the single-point findings obtained for this occupational study population.

Conclusions

Occupational populations with older age, higher BMI, and NAFLD should be considered symptomatic of GSD. Additional studies are required not only to discuss the temporal sequence of events lead to GSD development, but also to explore the clinical pathogenesis of GSD in this professional populations.

Conflict of Interest

No conflict of interest was declared by the authors.

Author Contributions

Execution of study and drafting of manuscript—T-H.T., W-H.C., R-C.C.; Study design and statistical analyses—J.W., T-H.T.; Study concept and coordination of manuscript drafting—J.W., F-L.C. All authors have read and approved the final version of the manuscript.

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Table 1. The gender and age specific prevalence of gallstone disease (n=8,352)

	Men (n=5,243)				Women (n=3,109)				Total (n=8,352)			
Age (yrs)	Screened No	GSD No	Prevalence (%)	P-value for trend test	Screened No	GSD No	Prevalence (%)	P-value for trend test	Screened No	GSD No	Prevalence (%)	P-value for trend test
<30	1152	10	0.87	<0.001	738	8	1.08	<0.001	1890	18	0.95	<0.001
30-39	1982	57	2.88		1100	35	3.18		3082	92	2.99	
40-49	1149	65	5.66		807	41	5.08		1956	106	5.42	
≧50	960	69	7.19		464	40	8.62		1424	109	7.65	
Total	5243	201	3.83		3109	124	3.99		8352	325	3.89	

Table 2 Crude and adjusted odds ratio of associated factors for GSD among screened population (n=8,352)

		GSD		Crude odds ratio (95% CI)	Adjusted odds ratio[1](95% CI)
		with (n=325)	without (n=8,027)		
Sex	Women	124	2985	1.00	---
	Men	201	5042	0.96 (0.76-1.20)	---
Age	<30	18	1872	1.00	---
	30-39	92	2990	3.20 (1.93-5.32)	---
	40-49	106	1850	5.96 (3.60-9.86)	---
	≧50	109	1315	8.62 (5.21-14.26)	---
Occupational professions	Computer and Mathematical	32	1299	1.00	---
	Architecture and Engineering	34	823	1.68 (1.03-2.74)	0.88 (0.53-1.47)
	Community and Social Service	27	626	1.75 (1.04-2.95)	0.89 (0.52-1.54)
	Sales and related	41	902	1.85 (1.15-2.95)	1.21 (0.74-1.97)
	Office and Administrative Support	132	2690	1.99 (1.35-2.95)	0.76 (0.49-1.18)
	Production	59	1687	1.42 (0.92-2.20)	1.07 (0.69-1.66)
Hypertension	no	253	6975	1.00	---
	yes	72	1052	1.89 (1.44-2.47)	1.26 (0.95-1.68)
Higher BMI	<**24**	136	4479	1.00	---
	24-27	89	2037	1.44 (1.10-1.89)	1.25 (0.94-1.65)
	≧27	100	1511	2.18 (1.67-2.84)	1.86 (1.42-2.45)
Hyperuricemia	no	178	4554	1.00	---
	yes	147	3473	1.08 (0.87-1.35)	1.16 (0.92-1.47)
Higher creatinine	no	305	7244	1.00	---
	yes	20	783	0.61 (0.38-0.96)	0.85 (0.53-1.35)
Higher AST	no	294	7515	1.00	---
	yes	31	512	1.55 (1.06-2.27)	1.32 (0.90-1.95)
Higher ALT	no	252	6751	1.00	---
	yes	73	1276	1.53 (1.17-2.00)	1.48 (1.12-1.95)
Higher ALP	no	281	6908	1.00	---
	yes	44	1119	0.97 (0.70-1.33)	1.18 (0.85-1.64)
Hypercholesterolemia	no	192	5157	1.00	---
	yes	133	2870	1.25 (0.99-1.56)	0.96 (0.76-1.21)
Hypertriglyceridemia	no	230	6153	1.00	---
	yes	95	1874	1.36 (1.06-1.73)	1.11 (0.86-1.43)
Higher fasting plasma glucose	no	303	7648	1.00	---
	yes	22	379	1.47 (0.94-2.29)	1.18 (0.96-1.37)
Nonalcoholic fatty liver disease	no	126	4190	1.00	---
	yes	199	3837	1.73 (1.37-2.17)	1.37 (1.08-1.74)

[1]Aujestment for gender and age

Table 3. Multiple logistic regression of associated factors for gallstones stratified by BMI (n=8,352)

	BMI<24		24≦BMI<27		27≦BMI		Tota1	
	(n=4615)		(n=2126)		(n=1611)		(n=8352)	
Variables	OR	95% CI	OR	95% CI	OR	95% CI	OR	95%CI
Sex (men vs. women)	0.78	0.55-1.11	0.86	0.52-1.43	0.77	0.49-1.22	0.81	0.63-1.03
AGE(yrs)	1.07	1.05-1.09	1.05	1.03-1.07	1.05	1.03-1.07	1.06	1.05-1.07
BMI (24-27 vs. <24 Kg/m^2)	----	----	----	----	----	----	1.18	0.87-1.61
(≧27 vs. <24 Kg/m^2)	----	----	----	----	----	----	1.70	1.12-2.34
Higher ALT (yes vs. no)	0.95	0.48-1.87	1.57	0.95-2.59	1.23	0.79-1.90	1.25	0.93-1.67
Nonalcoholic fatty liver disease (yes vs. no)	1.47	1.01-2.14	0.80	0.49-1.30	0.60	0.33-1.11	1.06	0.80-1.41

Table 4 Multiple logistic regression of associated factors for gallstone disease stratified by occupational professions (n=8,352)

	Office and Administrative Support (n=2822)	Architecture and Engineering (n=857)	Community and Social Service (n=653)	Sales and Related (n=943)	Computer and Mathematical (n=1331)	Production (n=1746)
	OR(95% CI)	OR(95% CI)	OR(95% CI)	OR(95% CI)	OR(95% CI)	OR(95% CI)
Sex (men vs. women)	0.77 (0.69-0.94)	0.85 (0.79-1.11)	0.89 (0.74-1.05)	0.80 (0.67-1.01)	0.84 (0.61-1.06)	0.74 (0.68-0.87)
Age (yrs)	1.05 (1.03-1.07)	1.07 (1.04-1.10)	1.03 (1.00-1.06)	1.07 (1.04-1.11)	1.05 (1.03-1.07)	1.03 (1.01-1.05)
Hypertension (yes vs. no)	1.19 (0.95-1.58)	1.20 (0.88-1.60)	1.09 (0.81-1.49)	1.12 (0.80-1.42)	1.15 (0.77-1.53)	1.09 (0.90-1.28)
BMI (24-27 vs. <24 Kg/m^2)	1.13 (0.83-1.45)	1.24 (1.02-1.43)	1.12 (0.91-1.35)	1.17 (1.01-1.48)	1.03 (0.94-1.15)	1.20 (0.97-1.48)
(≧27 vs. <24 Kg/m^2)	1.52 (1.19-1.90)	2.15 (1.28-3.07)	2.48 (1.53-3.24)	1.40 (1.08-1.73)	1.77 (1.46-2.08)	1.67 (1.49-1.80)
Hyperuricemia (yes vs. no)	1.18 (0.96-1.34)	1.12 (0.88-1.39)	1.09 (0.99-1.31)	1.06 (0.92-1.35)	1.16 (0.88-1.44)	1.12 (0.93-1.30)
Higher ALT (yes vs. no)	1.34 (1.12-1.59)	1.26 (0.97-1.55)	0.99 (0.86-1.13)	1.03 (0.90-1.19)	1.27 (1.13-1.44)	1.22 (0.98-1.49)
Hypercholesterolemia (yes vs. no)	1.04 (0.95-1.16)	1.17 (0.92-1.40)	0.87 (0.71-1.04)	0.96 (0.88-1.05)	1.02 (0.94-1.11)	1.05 (0.90-1.23)
Hypertriglyceridemia (yes vs. no)	1.09 (0.87-1.32)	0.97 (0.90-1.04)	1.13 (0.99-1.30)	1.06 (0.91-1.24)	0.99 (0.89-1.10)	1.05 (0.88-1.23)
Higher fasting plasma glucose (yes vs. no)	1.17 (1.22-2.62)	1.13 (1.02-1.26)	1.05 (0.96-1.17)	1.07 (0.91-1.24)	1.05 (0.96-1.14)	1.03 (0.77-1.30)
Nonalcoholic fatty liver disease(yes vs. no)	1.17 (1.02-1.33)	1.03 (0.92-1.15)	1.05 (0.94-1.18)	1.10 (1.01-1.20)	1.11 (1.03-1.22)	1.03 (0.97-1.09)

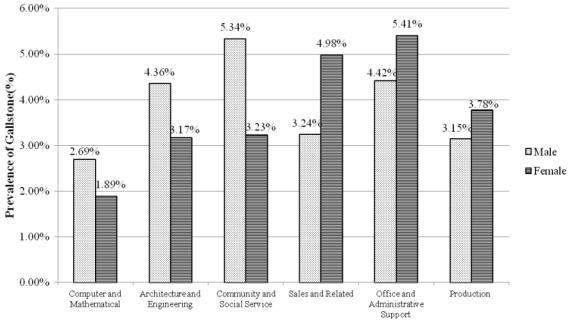

Figure 1 Prevalence of gallstone disease stratified by occupational professions

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